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L4           0 CDLVDGRCCCCRGDVLDC/SQSP

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L5          59 CCRGDVLD/SQSP

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L6           1 L5 AND CYC?

=> d l5

L5   ANSWER 1 OF 59  REGISTRY  COPYRIGHT 2007 ACS on STN
RN   943175-04-0  REGISTRY
ED   Entered STN:  23 Jul 2007
CN   α-Fetoprotein (human gene AFP precursor)  (CA INDEX NAME)
OTHER NAMES:
CN   6: PN: US20070154955 SEQID: 6 claimed protein
FS   PROTEIN SEQUENCE
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   CA, CAPLUS, USPATFULL

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)


=> d l5 sqide, nte

L5   ANSWER 1 OF 59  REGISTRY  COPYRIGHT 2007 ACS on STN
RN   943175-04-0  REGISTRY
CN   α-Fetoprotein (human gene AFP precursor)  (CA INDEX NAME)
OTHER NAMES:
CN   6: PN: US20070154955 SEQID: 6 claimed protein
FS   PROTEIN SEQUENCE
SQL  609

PATENT ANNOTATIONS (PNTE):
Sequence |Patent
Source   |Reference
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Not Given|US2007154955
         |claimed SEQID
         |6


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                               == ======
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       601 SKTRAALGV
HITS AT:   269-276

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   CA, CAPLUS, USPATFULL
DT.CA  CAplus document type:  Patent
RL.P   Roles from patents:  ANST (Analytical study); PRP (Properties); USES
       (Uses)
              1 REFERENCES IN FILE CA (1907 TO DATE)
              1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
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=> s ccrgdvld/sqsp
L1          59 CCRGDVLD/SQSP

=> s l1 and (cyc?/nte or cyc?)
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L1          59 CCRGDVLDC/SQSP

=> s ccrgdvld{1-3}[vlw]{1-3}[deg]/sqsp
INVALID USE OF BRACE OPERATOR

=> help
The arrow (=>) is the system prompt, where you enter a command.  For
an explanation of system commands, files, formats, etc., enter "HELP"
and the name of the item you want explained at an arrow prompt (=>).
Enter "HELP COMMANDS" for a list of commands that can be used in this
file.  Enter "HELP MESSAGES" for a list of online explanations that
are available.  The "?" can be used as a synonym for "HELP".

Help is also available at any prompt, and after any error message.
Enter "HELP" or "?" at a prompt to see an explanation of the options.
After an error message, enter "HELP" or "?" at the next prompt and you
will receive a more detailed explanation of the error and how to
correct it.

Automatic help is also available.  When AUHELP is 'ON', you will
automatically receive help following an error message.  For more
information on AUHELP, enter "HELP SET AUHELP" at an arrow
prompt (=>).

Users who need additional assistance can contact the Help Desk at
their nearest STN Service Center.  Enter "HELP STN" for information on
STN Service Centers.  You may also choose to contact the database
representative for the file you are searching, for more detailed help
on database content and search strategy.  For information on how to
contact database representatives for the current file, enter "HELP
DESK" at an arrow prompt (=>).

=> s ccrgdvld{1,3}[vlw]{1-3}[deg]/sqsp
INVALID USE OF BRACE OPERATOR

=> s ccrgdvld{1,3}[vlw]{1,3}[deg]/sqsp
INVALID USE OF BRACE OPERATOR

=> s ccrgdvl[d]{1-3}[vlw]{1-3}[deg]/sqsp
INVALID USE OF BRACE OPERATOR

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'CYCLIC' MUST END IN '/Q', '/A', '/L', '/S' OR '/B'
The saved name for a query (or structure or screen set) must end with
'/Q'.  The saved name for an answer set must end with '/A'.  The saved
name for an L# list must end with '/L'.  SDI request names must end
with '/S'.  To see a list of all saved query, answer set,, and L# list
names for this loginid, enter "DISPLAY SAVED" at an arrow
prompt (=>).  Enter "DISPLAY SAVED/S" to see a list of SDI request
names.  Enter "DISPLAY SAVED/B" to see a list of BATCH search
requests.

=> d l1 1, 3, 5, 7, 9 sqide

L1   ANSWER 1 OF 59  REGISTRY  COPYRIGHT 2007 ACS on STN
RN   943175-04-0  REGISTRY
CN   α-Fetoprotein (human gene AFP precursor)  (CA INDEX NAME)
OTHER NAMES:
CN   6: PN: US20070154955 SEQID: 6 claimed protein
FS   PROTEIN SEQUENCE
SQL  609
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PATENT ANNOTATIONS (PNTE):

Sequence Source	Patent Reference
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       601 SKTRAALGV
HITS AT:    269-277
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RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: ANST (Analytical study); PRP (Properties); USES (Uses)
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 3 OF 59 REGISTRY COPYRIGHT 2007 ACS on STN
RN 934655-59-1 REGISTRY
CN 9: PN: WO2006009492 FIGURE: 2B-2G unclaimed sequence (CA INDEX NAME)
FS PROTEIN SEQUENCE
SQL 675

PATENT ANNOTATIONS (PNTE):

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HITS AT:    335-343
MF    Unspecified
CI    MAN
SR    CA
LC    STN Files:    CA, CAPLUS
DT.CA  CAplus document type:  Patent
RL.P   Roles from patents:  PRP (Properties)
               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1    ANSWER 5 OF 59  REGISTRY  COPYRIGHT 2007 ACS on STN
RN    918921-82-1  REGISTRY
CN    2: PN: JP2007010567 SEQID: 4 unclaimed protein  (CA INDEX NAME)
FS    PROTEIN SEQUENCE
SQL   609

PATENT ANNOTATIONS (PNTE):
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       601 SKTRAALGV
HITS AT:    269-277

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**
MF    Unspecified
CI    MAN
SR    CA
LC    STN Files:    CA, CAPLUS, TOXCENTER
DT.CA  CAplus document type:  Patent
RL.P   Roles from patents:  PRP (Properties)
               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1    ANSWER 7 OF 59  REGISTRY  COPYRIGHT 2007 ACS on STN
RN    885679-35-6  REGISTRY
CN    α-Fetoprotein [233-glutamine] (synthetic human MM-093) (9CI)  (CA
      INDEX NAME)
FS    PROTEIN SEQUENCE
SQL   591
NTE
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 type            ------ location ------         description
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bridge           Cys-130     - Cys-175     disulfide bridge
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bridge          Cys-206     - Cys-252     disulfide bridge
bridge          Cys-251     - Cys-259     disulfide bridge
bridge          Cys-271     - Cys-285     disulfide bridge
bridge          Cys-284     - Cys-295     disulfide bridge
bridge          Cys-366     - Cys-375     disulfide bridge
bridge          Cys-398     - Cys-493     disulfide bridge
bridge          Cys-443     - Cys-444     disulfide bridge
bridge          Cys-454     - Cys-467     disulfide bridge
bridge          Cys-482     - Cys-483     disulfide bridge
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HITS AT:   251-259

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**
MF   Unspecified
CI   MAN
SR   CAS Client Services

L1   ANSWER 9 OF 59  REGISTRY  COPYRIGHT 2007 ACS on STN
RN   871848-76-9  REGISTRY
CN   107-609-α-Fetoprotein (human precursor) (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   2: PN: WO2005121341 SEQID: 16 claimed protein
FS   PROTEIN SEQUENCE
SQL  459

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       351 CTSSYANRRP CFSSLVVDET YVPPAFSDDK FIFHKDLCQA QGVALQTMKQ
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MF   Unspecified
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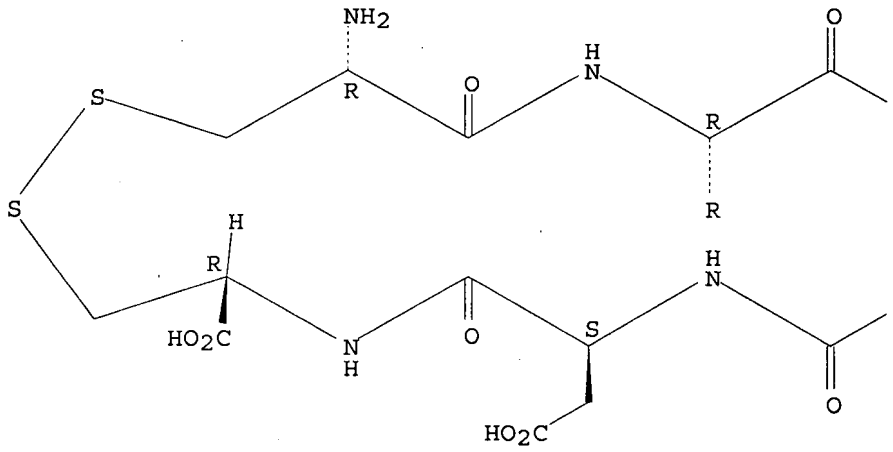
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PRP (Properties)
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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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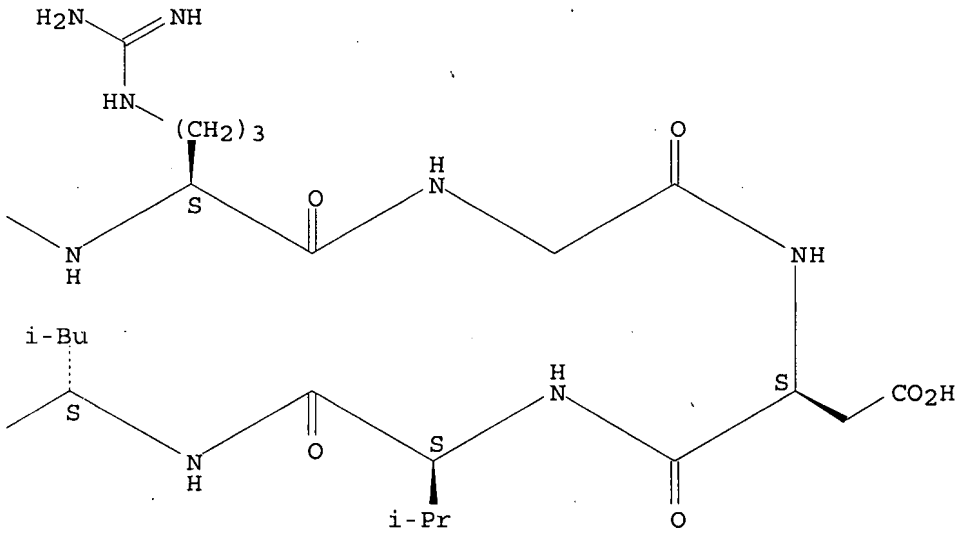
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RN 681481-25-4 REGISTRY
ED Entered STN: 13 May 2004
CN L-Cysteine, L-cysteinyl-L-cysteinyl-L-arginylglycyl-L-α-aspartyl-L-valyl-L-leucyl-L-α-aspartyl-, cyclic (1→9)-disulfide, bimol. (2→2')-disulfide (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C72 H118 N24 O28 S6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

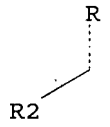
Absolute stereochemistry.



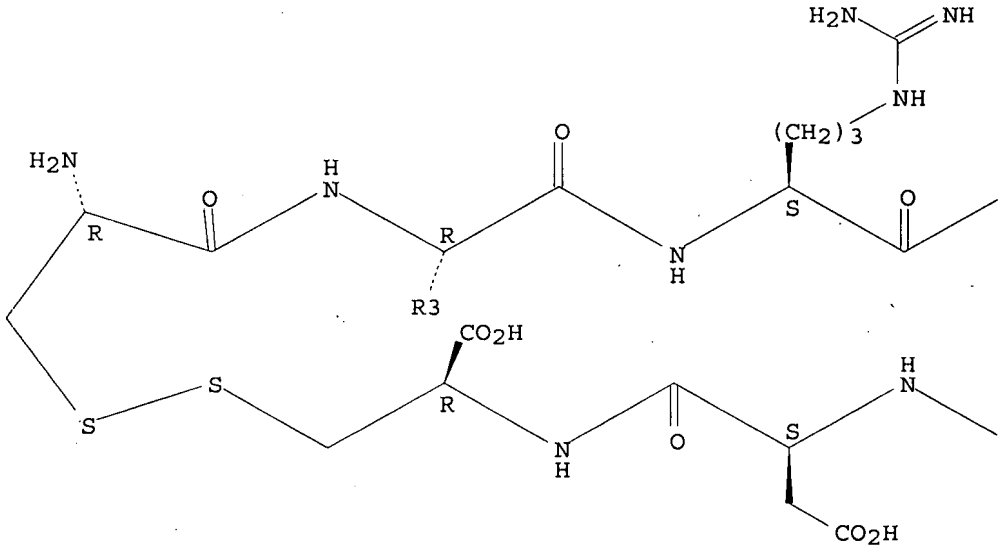
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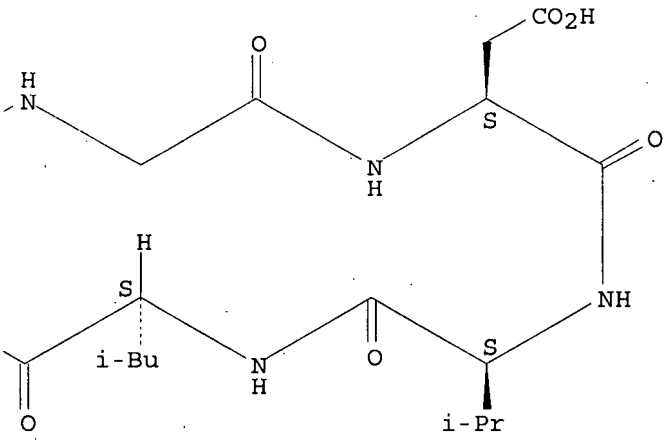


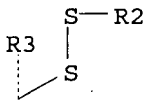
PAGE 2-A



PAGE 3-A







1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> d l2 nte

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN
NTE multichain

type	------ location ------		description
bridge	Cys-1	- Cys-9	disulfide bridge, dimer
bridge	Cys-2	- Cys-2'	disulfide bridge, dimer
bridge	Cys-1'	- Cys-9'	disulfide bridge, dimer

=> file hcaplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	76.30	76.51

FILE 'HCAPLUS' ENTERED AT 13:00:56 ON 09 AUG 2007
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strictly prohibited.

FILE COVERS 1907 - 9 Aug 2007 VOL 147 ISS 7
FILE LAST UPDATED: 8 Aug 2007 (20070808/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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           350 CYCLICS
        323515 CYCLIC
                  (CYCLIC OR CYCLICS)
L4           1 L3 AND CYCLIC

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L4 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:333751 HCAPLUS <<LOGINID::20070809>>
DN 140:355862
TI Peptides modulating caspase activation and uses thereof in modulation of apoptosis
IN Dudich, Elena Ivanovna; Semenkova, Lidia Nikolaevna; Dudich, Igor Vyacheslavovitch; Tatulov, Edward Borisovitch; Zubov, Dmitry Lvovicth; Korpela, Timo Kalevi
PA Russia
SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004033500	A1	20040422	WO 2003-FI735	20031007
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	FI 2002001798	A	20040410	FI 2002-1798	20021009
	AU 2003271784	A1	20040504	AU 2003-271784	20031007
	EP 1558649	A1	20050803	EP 2003-753618	20031007
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	CN 1703428	A	20051130	CN 2003-80101165	20031007
	JP 2006518703	T	20060817	JP 2004-542524	20031007
	US 2006280732	A1	20061214	US 2005-530779	20050408
	IN 2005KN00764	A	20060526	IN 2005-KN764	20050429
PRAI	FI 2002-1798	A	20021009		

WO 2003-FI735 W 20031007
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

FILE 'REGISTRY' ENTERED AT 15:35:11 ON 21 AUG 2007
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 20 AUG 2007 HIGHEST RN 945102-95-4
DICTIONARY FILE UPDATES: 20 AUG 2007 HIGHEST RN 945102-95-4

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TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

L1 59 S CCRGDVLD/SQSP
L2 6 S L1 AND (BRIDG? OR CYCL?)/NTE

FILE 'CAPLUS' ENTERED AT 15:35:11 ON 21 AUG 2007
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FILE COVERS 1907 - 21 Aug 2007 VOL 147 ISS 9
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L3 5 L2

L3 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:569608 CAPLUS Full-text
DOCUMENT NUMBER: 147:180938
TITLE: A randomised, double-blind, placebo-controlled trial of a recombinant version of human α-fetoprotein (MM-093) in patients with

active rheumatoid arthritis
AUTHOR(S): Pollard, L. C.; Murray, J.; Moody, M.; Stewart, E. J.; Choy, E. H. S.
CORPORATE SOURCE: Sir Alfred Baring Garrod Clinical Trials Unit, Academic Department of Rheumatology, King's College London, London, UK
SOURCE: Annals of the Rheumatic Diseases (2007), 66(5), 687-689
CODEN: ARDIAO; ISSN: 0003-4967
PUBLISHER: BMJ Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: Rheumatoid arthritis (RA) tends to remit during pregnancy, with more patients achieving remission in the third trimester, coinciding with an increase in levels of α-fetoprotein (AFP). In vitro and animal studies have shown that AFP has immunomodulatory properties. MM-093 is a non-glycosylated, recombinant version of human AFP. Objective: To assess the safety, tolerability and clin. effects of MM-093 during a 12-wk, randomized, double-blind, placebo-controlled study. Methods: 12 patients with RA, who had active disease and were on stable doses of methotrexate, received weekly s.c. injections of placebo or 21 mg of MM-093. Assessments were carried out at baseline and weekly thereafter. Results: Baseline characteristics were similar in both groups. There was one dropout in the placebo group, due to flare of disease. Treatment with MM-093 was well tolerated. No serious adverse event was observed By day 85, MM-093 produced a significant mean improvement from baseline in Disease Activity Score 28 (DAS28; 0.913 vs 0.008, p = 0.033) and patient's global assessment (28.9% vs -36.3%, p = 0.02) compared with placebo. Conclusion: This is the first randomized, controlled trial of MM-093, a recombinant version of human AFP, in patients with RA. MM-093 was well tolerated. Evidence of efficacy was observed, suggesting that MM-093 may have therapeutic potential in RA.

IT 885679-35-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(recombinant version of human α-fetoprotein, MM-093 was effective and safe in patient with active rheumatoid arthritis)
RN 885679-35-6 CAPLUS
CN α-Fetoprotein [233-glutamine] (synthetic human MM-093) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:333751 CAPLUS Full-text
DOCUMENT NUMBER: 140:355862
TITLE: Peptides modulating caspase activation and uses thereof in modulation of apoptosis
INVENTOR(S): Dudich, Elena Ivanovna; Semenkova, Lidia Nikolaevna; Dudich, Igor Vyacheslavovitch; Tatulov, Edward Borisovitch; Zubov, Dmitry Lvovicth; Korpela, Timo Kalevi
PATENT ASSIGNEE(S): Russia
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

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WO 2004033500	A1	20040422	WO 2003-FI735	20031007
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
FI 2002001798	A	20040410	FI 2002-1798	20021009
AU 2003271784	A1	20040504	AU 2003-271784	20031007
EP 1558649	A1	20050803	EP 2003-753618	20031007
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1703428	A	20051130	CN 2003-80101165	20031007
JP 2006518703	T	20060817	JP 2004-542524	20031007
US 2006280732	A1	20061214	US 2005-530779	20050408
IN 2005KN00764	A	20060526	IN 2005-KN764	20050429
PRIORITY APPLN. INFO.:			FI 2002-1798 A	20021009
			WO 2003-FI735 W	20031007

AB The present invention provides structures of small mols. capable of modulating apoptotic cell death. More specifically, the structures relate to the structures of apoptotic active sites of mammalian α-fetoprotein (AFP) and albumin. Peptides mimicking the active site contain two sequences, Arg-Gly-Asp and Asp-X-X-Asp, wherein X means any amino acid. These sequences are needed in the same mol. for causing a wide range of biol. activities. The peptides can be utilized to suppress apoptotic pathways by inhibiting the cytochrome c-mediated caspase activation. Thus, the peptides can be used to inhibit effects of apoptosis induced by oxidative stress, drugs, cytokines, Fas-ligand, α-fetoprotein, used to prevent apoptosis in culturing cells, in organ transplantation, in autoimmune disorders and immunodeficiency syndrome induced by viral infection, or to diminish cytotoxic side effects after chemotherapy and radiation therapy. The invention also discloses the preparation of anti-idiotypic antibodies against an apoptosis-active site of human α fetoprotein localized at amino acids 251-259 and at amino acids 246-254 of human serum albumin. Also prepared were antibodies to the mol. recognition site of a Fab fragment of anti-α fetoprotein and anti-albumin anti-idiotypic antibodies which were able to bind the above mentioned peptides.

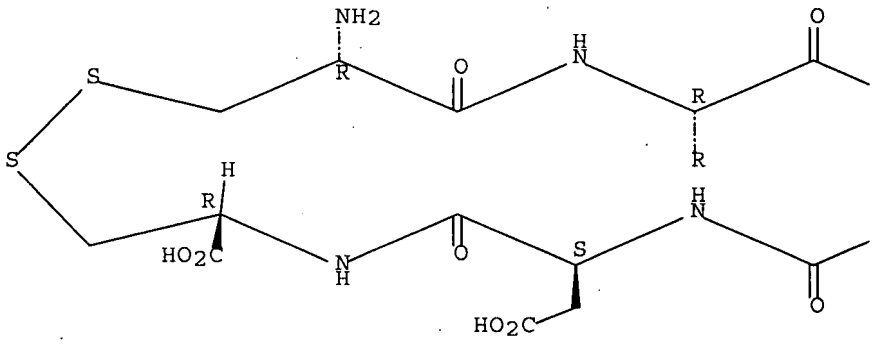
IT **681481-25-4**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (peptides modulating caspase activation and uses thereof in modulation of apoptosis)

RN 681481-25-4 CAPLUS

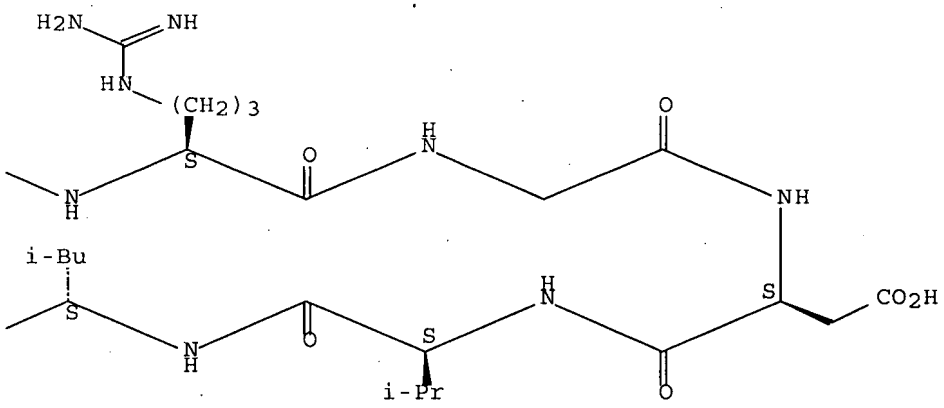
CN L-Cysteine, L-cysteinyl-L-cysteinyl-L-arginylglycyl-L-α-aspartyl-L-valyl-L-leucyl-L-α-aspartyl-, cyclic (1→9)-disulfide, bimol. (2→2')-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

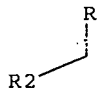
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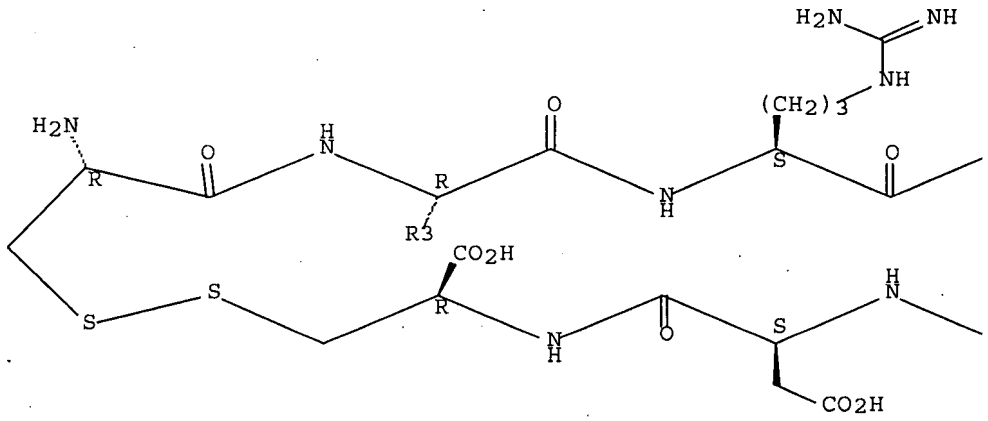
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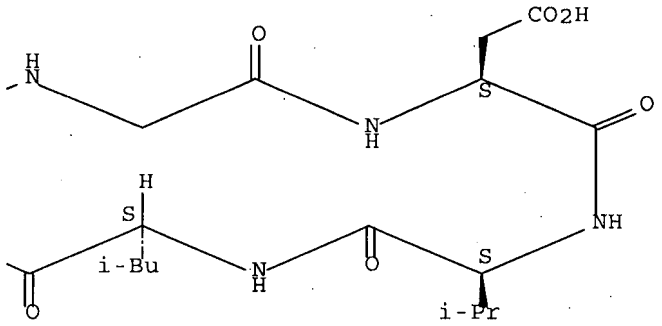
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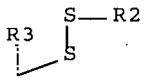
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PAGE 3-B



PAGE 4-A



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:167450 CAPLUS Full-text
DOCUMENT NUMBER: 116:167450
TITLE: Structure of the gorilla α-fetoprotein gene and the divergence of primates
AUTHOR(S): Ryan, Susan C.; Zielinski, Rita; Dugaiczyk, Achilles
CORPORATE SOURCE: Dep. Biochem., Univ. California, Riverside, CA, 92521, USA

SOURCE: Genomics (1991), 9(1), 60-72
CODEN: GNMCEP; ISSN: 0888-7543
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The sequence of the gorilla α-fetoprotein gene, including 869 base pairs of the 5' flanking region and 4892 base pairs of the 3' flanking region (24,607 in total), was determined from 2 overlapping lambda phage clones. The sequence extends 18,846 base pairs from the Cap site to the polyadenylation site, and it reveals that the gene is composed of 15 exons, which are sym. placed within 3 domains of α-fetoprotein. The deduced polypeptide chain is composed of a 19-amino-acid leader peptide, followed by 590 amino acids of the mature protein. The RNA polymerase II binding site, TATAAAA, and the promoter element, CCAAC, are positioned at -21 and -65 from the Cap site, resp. The polyadenylation signal, AATAAA, is located in the last exon, which is untranslated. The sequence for the gorilla α-fetoprotein gene was compared with that of the previously published human α-fetoprotein gene (P. E. M. Gibbs, et al., 1987). Four types of repetitive sequence elements were found in identical positions in both species. However, one Alu and one Xba DNA repeat within introns 4 and 7, resp., of the human gene are absent from orthologous positions in the gorilla. The Alu and the Xba DNA repeats probably emerged in the human genome after the human/gorilla divergence and became established novelties in the human lineage. There are 363/21,523 mutational changes between human and gorilla, amounting to 1.69% DNA divergence between the 2 primate species. The value of 1.69% is lower than the 2.27% obtained from melting temps. of hybrids between human and gorilla genomic DNA (Sibley, C. G., et al., 1984). At the protein level, Homo sapiens differs from Gorilla gorilla only at 4 of 609 amino acid positions (0.66%) in the α-fetoprotein sequence. This difference signifies a lower rate of mol. divergence for the α-fetoprotein gene in primates, compared with rodents.

IT **139316-62-4**, α-Fetoprotein (Gorilla gorilla clone λG22/λG9 precursor protein moiety) **139316-64-6**, α-Fetoprotein (Gorilla gorilla clone λG22/λG9 protein moiety)
RL: PRP (Properties)
(amino acid sequence of)

RN 139316-62-4 CAPLUS
CN α-Fetoprotein (Gorilla gorilla clone λG22/λG9 precursor protein moiety) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 139316-64-6 CAPLUS
CN α-Fetoprotein (Gorilla gorilla clone λG22/λG9 protein moiety) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L3 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1987:97208 CAPLUS Full-text
DOCUMENT NUMBER: 106:97208
TITLE: Structure, polymorphism and novel repeated DNA elements revealed by a complete sequence of the human α-fetoprotein gene
AUTHOR(S): Gibbs, Peter E. M.; Zielinski, Rita; Boyd, Carol; Dugaiczyk, Achilles
CORPORATE SOURCE: Dep. Biochem., Univ. California, Riverside, CA, 92521, USA
SOURCE: Biochemistry (1987), 26(5), 1332-43
CODEN: BICHAW; ISSN: 0006-2960

DOCUMENT TYPE: Journal
LANGUAGE: English

AB The human α-fetoprotein gene spans 19,489 base pairs (bp) from the putative cap site to the polyadenylation site. It is composed of 15 exons separated by 14 introns, which are sym. placed within the 3 domains of α-fetoprotein. In the 5' region, a putative TATAAA box is at position -21, and a variant sequence, CCAAC, of the common CAT box is at -65. Enhancer core sequences GTGG(TTT/AAA)> are in introns 3 and 4, and several copies of glucocorticoid response sequences AGA(T/A)CAG(T/A) are on the template strand of the gene. There are six polymorphic sites within 4690 bp of contiguous DNA derived from 2 allelic α-fetoprotein genes. This amts. to a measured polymorphic frequency of 0.13%, or 6.4 + 10-4/site, which is .apprx.5-10-fold lower than values estimated from studies on polymorphic restriction sites in other regions of the human genome. There are 4 types of repetitive sequence elements in the introns and flanking regions of the human α-fetoprotein gene. At least one of these is apparently a novel structure (designated Xba) and is found as a pair of direct repeats, with 1 copy in intron 7 and the other in intron 8. Apparently, within the last 2 million years, the copy in intron 8 gave rise to the repeat in intron 7. Their present location on both sides of exon 8 gives these sequences a potential for disrupting the functional integrity of the gene in the event of an unequal crossover between them. There are 3 Alu elements, one of which is in intron 4; the others are located in the 3'-flanking region. A solitary Kpn repeat is found in intron 3. The Xba and Kpn repeats were only detected by complete sequencing of the introns. Neither X, Xba, nor Kpn elements are present in the related human albumin gene, whereas Alu's are present in different positions. From phylogenetic evidence it appears that Alu elements were inserted into the α-fetoprotein gene at some time postdating the mammalian radiation 85 million years ago.

IT **87501-57-3 87501-58-4**
RL: PRP (Properties)
(amino acid sequence of)

RN 87501-57-3 CAPLUS

CN α-Fetoprotein (human precursor protein moiety) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 87501-58-4 CAPLUS

CN α-Fetoprotein (human protein moiety) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L3 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1983:553084 CAPLUS Full-text
DOCUMENT NUMBER: 99:153084
TITLE: Primary structures of human α-fetoprotein and its mRNA
AUTHOR(S): Morinaga, Tomonori; Sakai, Masaharu; Wegmann, Thomas G.; Tamaoki, Taiki
CORPORATE SOURCE: Dep. Med. Biochem., Univ. Calgary, Calgary, AB, T2N 4N1, Can.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1983), 80(15), 4604-8
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB DNA complementary to human α-fetoprotein (AFP) mRNA was cloned in plasmid pBR322. Anal. of 3 overlapping cDNA clones revealed most of the nucleotide sequence of AFP mRNA, and the remaining nucleotides at the 5' end of the mRNA

were elucidated from a cloned genomic DNA fragment. The amino acid sequence was deduced from the nucleotide sequence and revealed 19 amino acids in the signal sequence and 590 amino acids in mature AFP. There are 15 regularly spaced disulfide bridges, which generate a folding structure having 3 repeating domains. There is 1 potential N-glycosylation site, Asn-Phe-Thr, in the amino acid sequence. In comparison with mouse AFP, 66% of the amino sequence was conserved, with the highest identity (72%) in domain 3, followed by domain 2 (67%) and domain 1 (59%). In comparison with human albumin, a 39% conservation of primary structure was found. Again, the similarity was the highest in domain 3 and the lowest in domain 1. Human AFP and human albumin are similar in overall structure, but certain parts of the mols. differ significantly in their predicted secondary structure.

IT 87501-57-3 87501-58-4
RL: PRP (Properties)
(amino acid sequence of)

RN 87501-57-3 CAPLUS

CN α-Fetoprotein (human precursor protein moiety) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 87501-58-4 CAPLUS

CN α-Fetoprotein (human protein moiety) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

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FILE LAST UPDATED: 01 May 1997 (19970501/UP)

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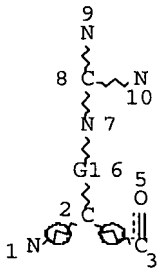
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L5 0 L1

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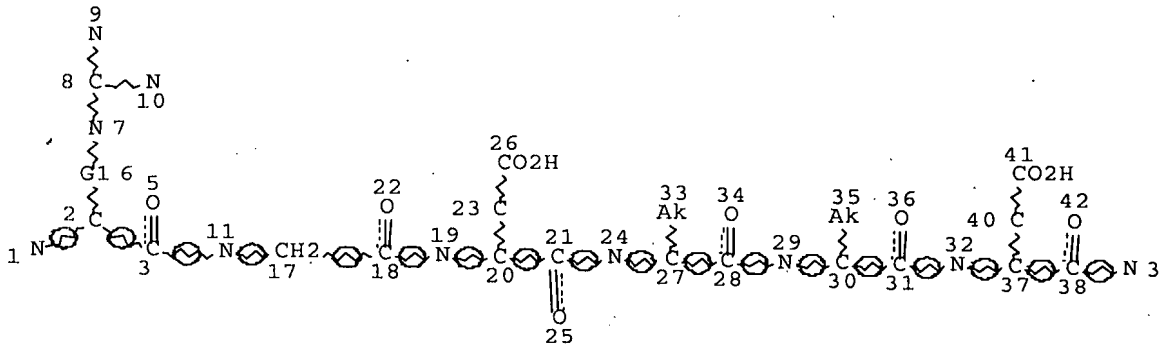
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Page 1-B
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FILE LAST UPDATED: 20 Aug 2007 (20070820/ED)

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L10 5 L9

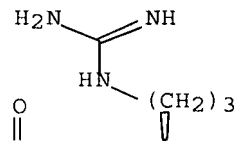
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L11 4 L10 NOT L3

L11 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:452605 CAPLUS Full-text
DOCUMENT NUMBER: 144:65623
TITLE: Structure and function of RGD peptides derived from disintegrin proteins
AUTHOR(S): Kim, Jiun; Hong, Sung-Yu; Park, Hye-seo; Kim, Doo-Sik; Lee, Weontae
CORPORATE SOURCE: Department of Biochemistry, Yonsei University, Seoul, 120-740, S. Korea
SOURCE: Molecules and Cells (2005), 19(2), 205-211
CODEN: MOCEEK; ISSN: 1016-8478
PUBLISHER: Korean Society for Molecular and Cellular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The Arg-Gly-Asp (RGD) sequence serves as the primary recognition site in extracellular matrix proteins, and peptides containing this sequence can mimic the biol. activities of matrix proteins. We have initiated structure-function studies of two RGD containing peptides, RGD-5(AGGDD) and cyclic RGD-6(CARGDDC). Assays have shown that cyclic RGD-peptides inhibit platelet aggregation more efficiently than linear ones. NMR data revealed that RGD-5 and RGD-6 have entirely different conformations. RGD-5 has a linear extended structure and RGD-6 has a stable loop conformation. In RGD-5 the guanidinium group of Arg2 and the carboxyl group of Asp4 lie in parallel, whereas the side-chains of Arg3 and Asp5 of RGD-6 are located in different planes, supporting the idea that the stability of the cyclic form derives from the packing of the side chain of the Arg and Asp residues. The structural features of these peptides could provide a basis for designing new drugs against diseases related to platelet aggregation and as cancer antagonists.

IT **872049-73-5**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(structure and function of RGD peptides derived from disintegrin proteins)
RN 872049-73-5 CAPLUS
CN L-Cysteinamide, N-acetyl-L-cysteinyl-L-arginyl-L-arginyl-L-alanyl-L-arginylglycyl-L-α-aspartyl-L-α-aspartyl-L-leucyl-L-α-aspartyl-L-α-aspartyl-L-leucyl-L-tyrosyl-, cyclic (1→14)-disulfide (9CI) (CA INDEX NAME)

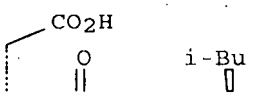
Absolute stereochemistry.

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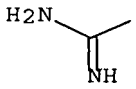




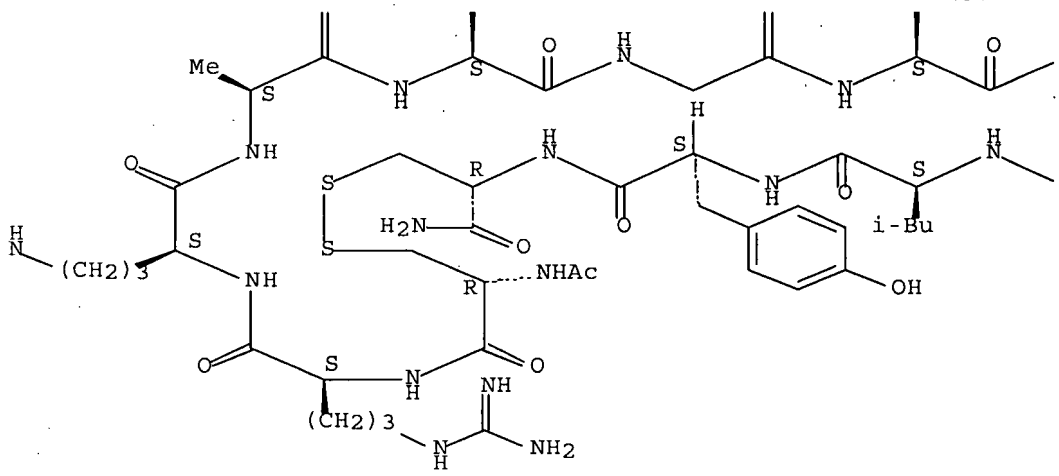
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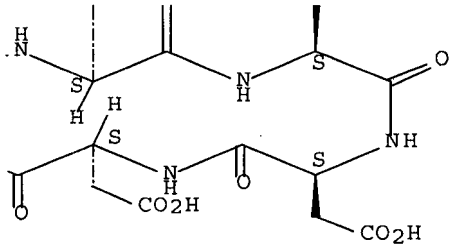
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PAGE 2-C



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L11 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:789404 CAPLUS Full-text
DOCUMENT NUMBER: 123:333284
TITLE: Novel integrin-binding peptides and their analytical and therapeutic uses in the control of

cellular adhesion

INVENTOR(S): Ruoslahti, Erkki; Koivunen, Erkki
PATENT ASSIGNEE(S): La Jolla Cancer Research Foundation, USA
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9514714	A1	19950601	WO 1994-US13542	19941122
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RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5981478	A	19991109	US 1994-286861	19940804
CA 2177070	A1	19950601	CA 1994-2177070	19941122
AU 9512596	A	19950613	AU 1995-12596	19941122
AU 682561	B2	19971009		
EP 730607	A1	19960911	EP 1995-903595	19941122
EP 730607	B1	20010530		
R: BE, CH, DE, DK, FR, GB, IT, LI, NL, SE				
JP 09509142	T	19970916	JP 1994-515220	19941122

PRIORITY APPLN. INFO.:
US 1993-158001 A 19931124
US 1994-286861 A 19940804
WO 1994-US13542 W 19941122

OTHER SOURCE(S): MARPAT 123:333284

AB Novel integrin-binding peptides that bind to αv- or α5-containing integrins and can exhibit high binding affinity. They contain one of the following sequence motifs: RX1ETX2WX3 (especially RRETAWA); RGDGX in which Xn is an amino acid with a hydrophobic, aromatic side chain; the double cyclic CX1CRGDCX2C; and RLD. The peptides generally exhibit their highest binding affinity when they assume a conformationally stabilized configuration, e.g. by cyclization through disulfide bonds. These peptides may be used as affinity labels for purification and anal. of integrins, e.g. in the testing of the efficacy of integrin-binding pharmaceuticals such as antithrombotics. These peptides may also be useful as substrates for attachment of integrin-bearing cells to surfaces such as prosthetic devices or in preventing the unwanted binding of cells to a target, such as the binding of osteoclasts to bone in the treatment of of osteoporosis; the inhibition of angiogenesis, and as tumor inhibitors. Integrin-binding peptides were obtained by affinity purification of a phage display library containing random sequences in the display cassette by panning with integrins. Peptides specific for several different classes of integrin were obtained.

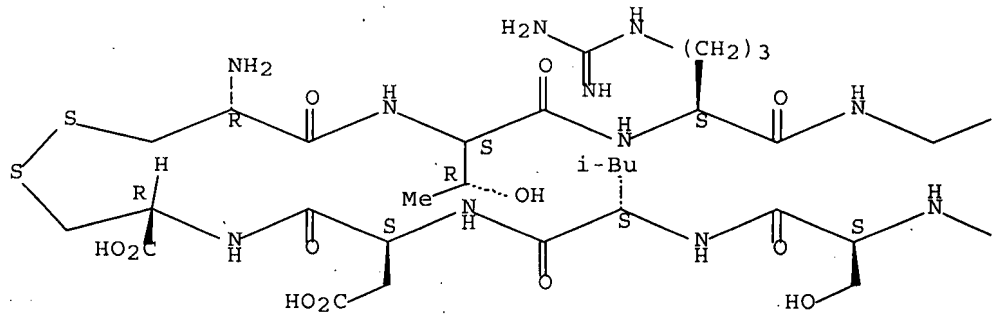
IT **168178-77-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(binding to αvβ1 integrin of; novel integrin-binding peptides and their anal. and therapeutic uses in control of cellular adhesion)

RN 168178-77-6 CAPLUS

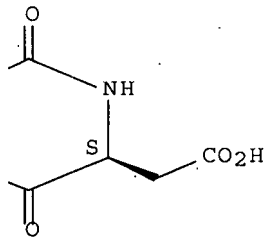
CN L-Cysteine, L-cysteinyl-L-threonyl-L-arginylglycyl-L-α-aspartyl-L-seryl-L-leucyl-L-α-aspartyl-, cyclic (1→9)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L11 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:440846 CAPLUS Full-text
DOCUMENT NUMBER: 119:40846
TITLE: Inhibition of osteoclastic bone resorption in vivo by echistatin, an "arginyl-glycyl-aspartyl" (RGD)-containing protein
AUTHOR(S): Fisher, John E.; Caulfield, Michael P.; Sato, Masahiko; Quartuccio, Helen A.; Gould, Robert J.; Garsky, Victor M.; Rodan, Gideon A.; Rosenblatt, Michael
CORPORATE SOURCE: Dep. Bone Biol. Osteoporosis, Merck Res. Lab., West Point, PA, 19486, USA
SOURCE: Endocrinology (1993), 132(3), 1411-13
CODEN: ENDOAO; ISSN: 0013-7227
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Osteolastic bone resorption requires the formation of a tightly sealed compartment between the osteoclast and the mineralized bone matrix. This compartment functions as an extracellular lysosome which contains proteolytic enzymes and acids. Vitronectin receptors (VnR, integrin αvβ3) displayed on

the osteoclast cell surface may play a role in the attachment of osteoclasts to the resorption surface. VnR are known to bind to arginyl-glycyl-aspartyl (RGD)-containing matrix proteins and it has recently been reported that soluble peptides containing RGD sequences can block osteoclast attachment to bone and inhibit bone resorption in vitro. Echistatin, a naturally-occurring protein containing an RGD-sequence motif, completely inhibited osteoclast-mediated bone resorption in vivo. Echistatin or smaller derivative peptides may prove useful in the treatment of disorders characterized by excess bone resorption, such as osteoporosis and metastatic bone disease.

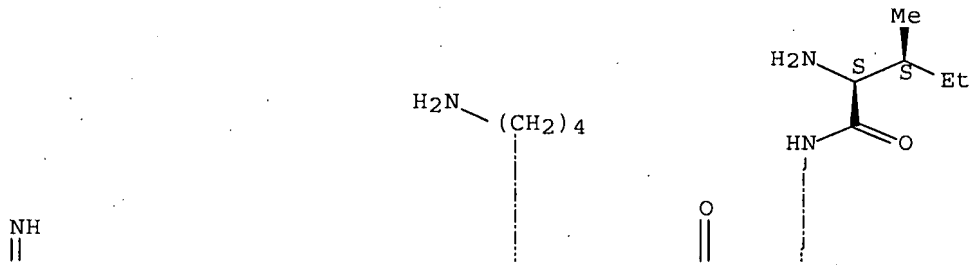
IT **148599-69-3**
RL: BIOL (Biological study)
(bone resorption inhibition by)

RN 148599-69-3 CAPLUS

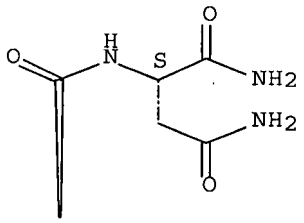
CN L-Aspartamide, L-isoleucyl-L-cysteinyl-L-lysyl-L-arginyl-L-alanyl-L-arginylglycyl-L-α-aspartyl-L-α-aspartyl-L-methionyl-L-α-aspartyl-L-α-aspartyl-L-tyrosyl-L-cysteinyl-, cyclic (2→14)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-B



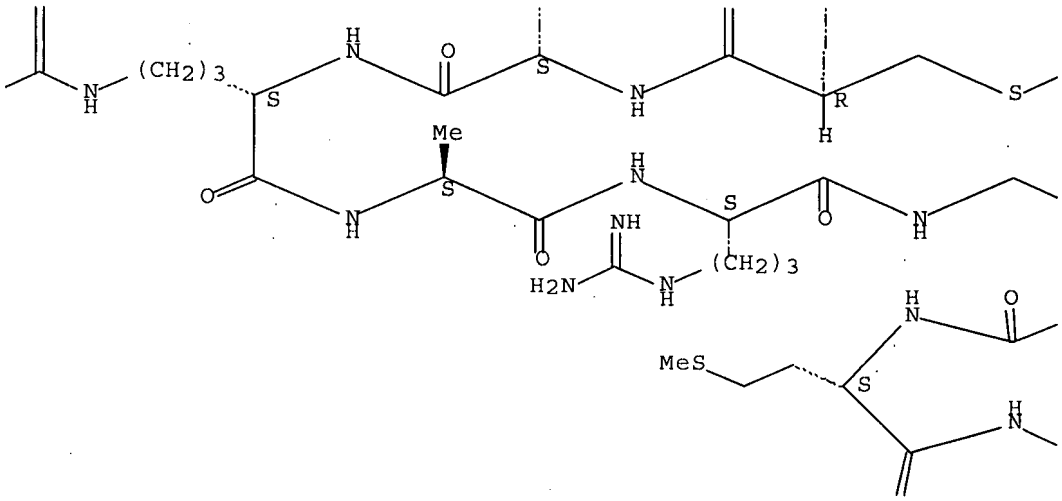
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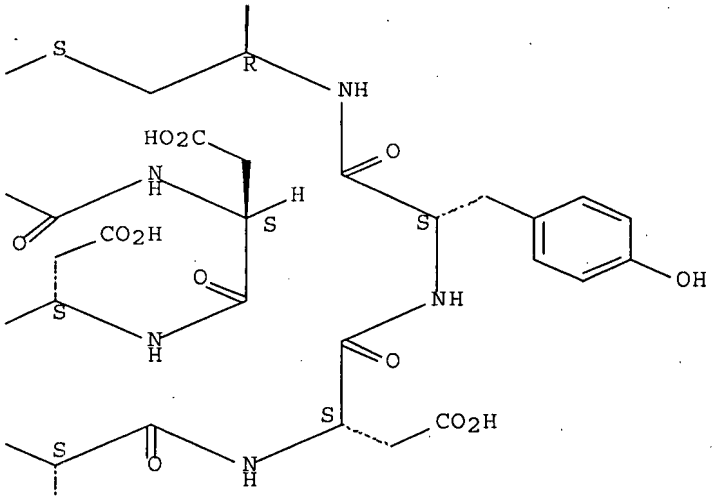
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H_2N

PAGE 2-B

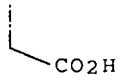


PAGE 2-C



PAGE 3-B

PAGE 3-C



L11 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	1991:656668 CAPLUS Full-text
DOCUMENT NUMBER:	115:256668
TITLE:	Preparation of cyclic peptides containing Arg-Gly-Asp flanked by proline as platelet aggregation inhibitors
INVENTOR(S):	Barker, Peter L.; Burnier, John P.; Lazarus, Robert A.
PATENT ASSIGNEE(S):	Genentech, Inc., USA
SOURCE:	PCT Int. Appl., 29 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

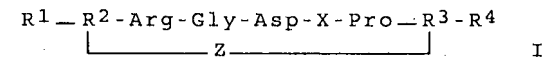
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9111458	A1	19910808	WO 1991-US564	19910128

W: CA, JP
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE

CA 2073696 A1 19910803 CA 1991-2073696 19910128
PRIORITY APPLN. INFO.: US 1990-474182 A 19900202

OTHER SOURCE(S): MARPAT 115:256668
GI



I

AB Title compds. (I; R1, R4 = 0-4 amino acids; R3 = 1-4 amino acids; R2 = CH2CO, 1-4 amino acids; X = Met, Phe, Leu, Ile, Asp, Lys, Arg, Gln, norleucine residue; Z = disulfide, thioether, or amide linkage), were prepared Thus, H-Cys-Arg-Ile-Pro-Arg-Gly-Asp-Met-Pro-Asp-Asp-Arg-Cys-OH cyclic disulfide (II) was prepared by peptide coupling on FMOC-Cyc(Trt) PepSyn KA resin followed by air oxidation of the linear peptide. II inhibited blood platelet aggregation with IC50 = 8 μM, and inhibited immobilized fibrinogen binding to G-P IIbIIIa with the IC50 ratio (II:H-Gly-Arg-Gly-Asp-Val-OH) of 0.5.

IT **137414-89-2P 137414-94-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as blood platelet aggregation inhibitor)

RN 137414-89-2 CAPLUS

CN L-Cysteine,.L-cysteinyl-L-arginyl-L-arginyl-L-alanyl-L-arginylglycyl-L-α-aspartyl-L-α-aspartyl-L-leucyl-L-α-aspartyl-L-α-aspartyl-L-tyrosyl-, cyclic (1→13)-disulfide (9CI) (CA INDEX NAME)

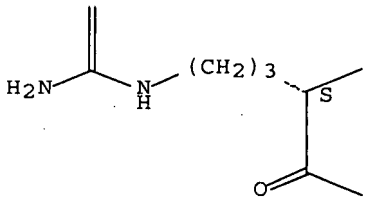
Absolute stereochemistry.

NH
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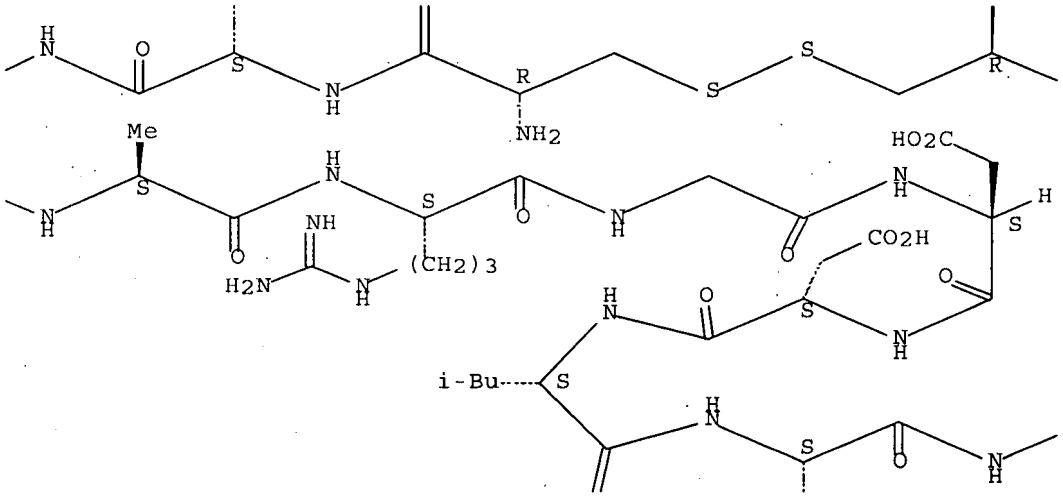
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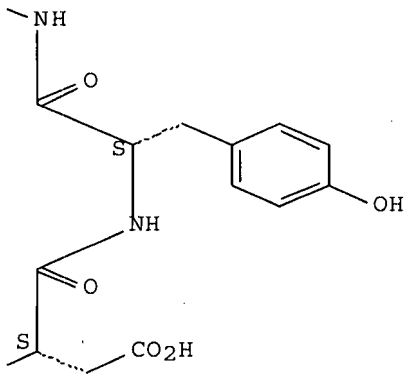
PAGE 2-A



PAGE 2-B



PAGE 2-C



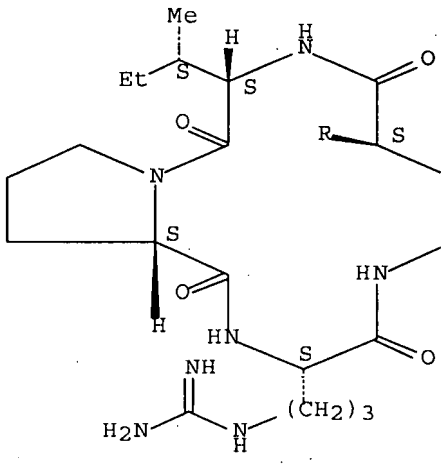
PAGE 3-B



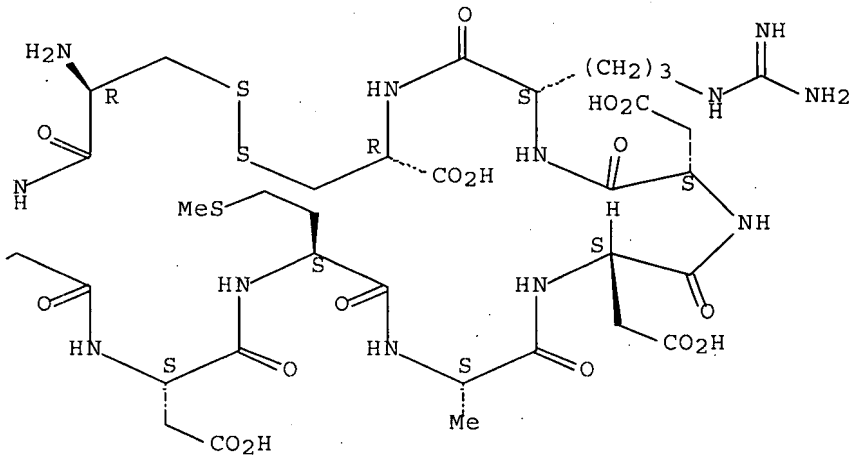
RN 137414-94-9 CAPLUS
CN L-Cysteine, L-cysteinyl-L-arginyl-L-isoleucyl-L-prolyl-L-arginylglycyl-L-α-aspartyl-L-methionyl-L-alanyl-L-α-aspartyl-L-α-aspartyl-L-arginyl-, cyclic (1→13)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

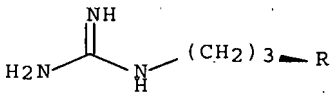
PAGE 1-B



PAGE 1-C



PAGE 2-A



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FILE LAST UPDATED: 01 May 1997 (19970501/UP)

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L13             0 L9

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L14           196 SEA ABB=ON  PLU=ON  "DUDICH E"?/AU
L15           121 SEA ABB=ON  PLU=ON  "SEMENKOVA L"?/AU
L16           177 SEA ABB=ON  PLU=ON  "DUDICH I"?/AU
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L18            71 SEA ABB=ON  PLU=ON  "ZUBOV D"?/AU
L19           568 SEA ABB=ON  PLU=ON  "KORPELA T"?/AU
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L23            43 SEA ABB=ON  PLU=ON  L16 AND (L17 OR L18 OR L19)
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                L19) OR (L21 OR L22 OR L23 OR L24)) AND (APOPTOS? OR
                APOPTOT? OR (CELL OR CELLULAR)(3A) DEATH)
L27            28 SEA ABB=ON  PLU=ON  L26 AND (AMINO OR PROTEIN OR POLYPROTEI
                N OR POLYPEPTIDE OR PEPTIDE)
L28            28 SEA ABB=ON  PLU=ON  L20 OR L25 OR L27
L29            12 DUP REM L28 (16 DUPLICATES REMOVED)

L29  ANSWER 1 OF 12  CAPLUS  COPYRIGHT 2007 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2006:898444  CAPLUS  Full-text
DOCUMENT NUMBER:          145:391081
TITLE:                    Alpha-fetoprotein antagonizes X-linked inhibitor
                          of apoptosis protein
                          anticaspase activity and disrupts XIAP-caspase
                          interaction
AUTHOR(S):                Dudich, Elena; Semenkova, Lidia
                          ; Dudich, Igor; Denesyuk, Alexander;
                          Tatulov, Edward; Korpela, Timo
```

CORPORATE SOURCE: Institute of Immunological Engineering, Lyubuchany, Russia
SOURCE: FEBS Journal (2006), 273(16), 3837-3849
CODEN: FJEOAC; ISSN: 1742-464X
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previous results have shown that the human oncoembryonic **protein** α-fetoprotein (AFP) induces dose-dependent targeting **apoptosis** in tumor cells, accompanied by cytochrome c release and caspase 3 activation. AFP pos. regulates cytochrome c/dATP-mediated **apoptosome** complex formation in a cell-free system, stimulates release of the active caspases 9 and 3 and displaces cIAP-2 from the **apoptosome** and from its complex with recombinant caspases 3 and 9. We suggested that AFP might affect the X-linked inhibitor of **apoptosis protein** (XIAP)-caspase interaction by blocking binding and activating the **apoptotic** machinery via abrogation of inhibitory signaling. We show here that AFP cancels XIAP-mediated inhibition of endogenous active caspases in cytosolic lysates of tumor cells, as well as XIAP-induced blockage of active recombinant caspase 3 in a reconstituted cell-free system. A direct **protein- protein** interaction assay showed that AFP phys. interacts with XIAP mol., abolishes XIAP-caspase binding and rescues caspase 3 from inhibition. The data suggest that AFP is directly involved in targeting pos. regulation of the **apoptotic** pathway dysfunction in cancer cells by inhibiting the **apoptosis** inhibitor **protein**, thereby triggering **apoptosis**.

REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2004:333751 CAPLUS Full-text
DOCUMENT NUMBER: 140:355862
TITLE: **Peptides** modulating caspase activation and uses thereof in modulation of **apoptosis**
INVENTOR(S): **Dudich, Elena Ivanovna; Semenkova, Lidia Nikolaevna; Dudich, Igor Vyacheslavovitch; Tatulov, Edward Borisovitch; Zubov, Dmitry Lvovicth ; Korpela, Timo Kalevi**
PATENT ASSIGNEE(S): Russia
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004033500	A1	20040422	WO 2003-FI735	20031007

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,

NE, SN, TD, TG

FI 2002001798	A	20040410	FI 2002-1798		20021009
AU 2003271784	A1	20040504	AU 2003-271784		20031007
EP 1558649	A1	20050803	EP 2003-753618		20031007
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
CN 1703428	A	20051130	CN 2003-80101165		20031007
JP 2006518703	T	20060817	JP 2004-542524		20031007
US 2006280732	A1	20061214	US 2005-530779		20050408
IN 2005KN00764	A	20060526	IN 2005-KN764		20050429
PRIORITY APPLN. INFO.:			FI 2002-1798	A	20021009
			WO 2003-FI735	W	20031007

AB The present invention provides structures of small mols. capable of modulating **apoptotic cell death.** More specifically, the structures relate to the structures of **apoptotic** active sites of mammalian α-fetoprotein (AFP) and albumin. **Peptides** mimicking the active site contain two sequences, Arg-Gly-Asp and Asp-X-X-Asp, wherein X means any **amino** acid. These sequences are needed in the same mol. for causing a wide range of biol. activities. The **peptides** can be utilized to suppress **apoptotic** pathways by inhibiting the cytochrome c-mediated caspase activation. Thus, the **peptides** can be used to inhibit effects of **apoptosis** induced by oxidative stress, drugs, cytokines, Fas-ligand, α-fetoprotein, used to prevent **apoptosis** in culturing cells, in organ transplantation, in autoimmune disorders and immunodeficiency syndrome induced by viral infection, or to diminish cytotoxic side effects after chemotherapy and radiation therapy. The invention also discloses the preparation of anti-idiotypic antibodies against an **apoptosis**-active site of human α fetoprotein localized at **amino** acids 251-259 and at **amino** acids 246-254 of human serum albumin. Also prepared were antibodies to the mol. recognition site of a Fab fragment of anti-α fetoprotein and anti-albumin anti-idiotypic antibodies which were able to bind the above mentioned **peptides.**

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2003:968778 CAPLUS Full-text
DOCUMENT NUMBER: 139:394145
TITLE: α-Fetoprotein positively regulates cytochrome c-mediated caspase activation and **apoptosome** complex formation
AUTHOR(S): **Semenkova, Lidia; Dudich, Elena ; Dudich, Igor;** Tokhtamisheva, Natalie; **Tatulov, Edward;** Okruzhnov, Yury; Garcia-Foncillas, Jesus; Palop-Cubillo, Juan-Antonio; **Korpela, Timo**
CORPORATE SOURCE: Inst. Immunological Eng., Moscow, Russia
SOURCE: European Journal of Biochemistry (2003), 270(21), 4388-4399
CODEN: EJBCAI; ISSN: 0014-2956
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previous results have shown that the oncoembryonic marker α-fetoprotein (AFP) is able to induce **apoptosis** in tumor cells through activation of caspase 3, bypassing Fas-dependent and tumor necrosis factor receptor-dependent signaling. In this study we further investigate the mol. interactions

involved in the AFP-mediated signaling of **apoptosis**. We show that AFP treatment of tumor cells is accompanied by cytosolic translocation of mitochondrial cytochrome c. In a cell-free system, AFP mediates processing and activation of caspases 3 and 9 by synergistic enhancement of the low-dose cytochrome c-mediated signals. AFP was unable to regulate activity of caspase 3 in cell exts. depleted of cytochrome c or caspase 9. Using high-resolution chromatog., we show that AFP pos. regulates cytochrome c/dATP-mediated **apoptosome** complex formation, enhances recruitment of caspases and Apaf-1 into the complex, and stimulates release of the active caspases 3 and 9 from the **apoptosome**. By using a direct **protein- protein** interaction assay, we show that pure human AFP almost completely disrupts the association between processed caspases 3 and 9 and the cellular inhibitor of **apoptosis protein** (cIAP-2), demonstrating its release from the complex. Our data suggest that AFP may regulate **cell death** by displacing cIAP-2 from the **apoptosome**, resulting in promotion of caspase 3 activation and its release from the complex.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 4 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:522058 BIOSIS Full-text
DOCUMENT NUMBER: PREV200300521989
TITLE: Synthetic **peptides** derived from human alpha-fetoprotein sequence functionally regulate **apoptosis** in tumor cells.
AUTHOR(S): **Dudich, E.** [Reprint Author]; **Semenkova, L.** [Reprint Author]; **Dudich, I.** [Reprint Author]; Tatoulov, E. [Reprint Author]; **Korpela, T.**
CORPORATE SOURCE: Institute Immunological Engineering, Lyubuchany, Moscow Region, 142380, Russia
SOURCE: Tumor Biology, (August 2003) Vol. 24, No. Supplement 1, pp. 53. print.
Meeting Info.: XXXIst Meeting of the International Society for Oncodevelopmental Biology and Medicine. Edinburgh, UK. August 30-September 04, 2003. International Society for Oncodevelopmental Biology and Medicine.
ISSN: 1010-4283 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Nov 2003
Last Updated on STN: 5 Nov 2003

L29 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:486729 CAPLUS Full-text
DOCUMENT NUMBER: 135:342150
TITLE: α-Fetoprotein-induced **apoptosis** of cancer cells
AUTHOR(S): **Dudich, E. I.**; **Semenkova, L. N.**; **Dudich, I. V.**; Nikolaeva, M. A.; Gorbatova, E. A.; Khromykh, L. M.; Grechko, G. K.; Sukhikh, G. T.
CORPORATE SOURCE: Institute of Engineering Immunology, Lyubuchany, Russia
SOURCE: Bulletin of Experimental Biology and Medicine (Translation of Byulleten Eksperimental'noi

Biologii i Meditsiny) (2001), Volume Date 2000, 130(12), 1127-1133
CODEN: BEXBAN; ISSN: 0007-4888
PUBLISHER: Consultants Bureau
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with refs. on the effects of human embryonic or cancer α-fetoprotein (AFP) on proliferative activity of cancer and normal cells and the evaluation in the mechanisms of AFP-induced **apoptosis.** The cytostatic activity of AFP did not depend on the ligands content, but was determined by the structure and properties of **protein** macromols. Human AFP produced a dose-dependent effect (activation or inhibition) on the growth of normal and tumor cells. AFP in low doses stimulated cell proliferation, while in high doses this substance caused pronounced cytostatic and cytotoxic effects on tumor cells. The effect of AFP was dependent on the presence of growth factors and cytokines in the culture medium, which attests to the interrelation between transduction of growth and **apoptotic** signal pathways. The suppression of cell growth, DNA degradation, and clear morphol. signs of programmed **cell death** characterized the AFP-induced **apoptosis.**

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 6 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:11178 BIOSIS Full-text
DOCUMENT NUMBER: PREV200100011178
TITLE: Alpha-fetoprotein-derived synthetic **peptide,** sharing Bcl2-homology, abrogates AFP-induced **apoptosis** in human tumour cells in vitro.
AUTHOR(S): **Dudich, Elena** [Reprint author]; Gorbatova, Elena [Reprint author]; Mizejewski, G. [Reprint author]
CORPORATE SOURCE: Institute of Engineering Immunology, Lyubuchany, Moscow Region, Russia
SOURCE: Tumor Biology, (September, 2000) Vol. 21, No. Supplement 1, pp. 109. print.
Meeting Info.: 28th Meeting of the International Society for Oncodevelopmental Biology and Medicine. Munich, Germany. September 08-13, 2000. International Society for Oncodevelopmental Biology and Medicine.
ISSN: 1010-4283.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Dec 2000
Last Updated on STN: 21 Dec 2000

L29 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 1999:459169 CAPLUS Full-text
DOCUMENT NUMBER: 131:253838
TITLE: Isolation and Structural and Functional Characterization of Two Stable Peptic Fragments of Human α-Fetoprotein
AUTHOR(S): **Dudich, Igor**; Tokhtamysheva, Natasha; **Semenkova, Lidia**; **Dudich, Elena**; Hellman, Jukka; **Korpela, Timo**
CORPORATE SOURCE: Institute of Engineering Immunology, Lyubuchany, 142380, Russia
SOURCE: Biochemistry (1999), 38(32), 10406-10414
CODEN: BICHAW; ISSN: 0006-2960

PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Short-time limited peptic hydrolysis of ligand-free human α-fetoprotein (AFP) gave two main fragments with mol. masses of 38 and 32 kDa, which had been produced by splitting of the mol. at the position Leu312-Asn313. A more prolonged proteolysis led to the further degradation of these fragments and appearance of highly proteolytically resistant 23-kDa (P23) and 26-kDa (P26) fragments, corresponding to N- and C-terminal parts of the AFP mol., resp. Comparative study of intact free of ligands AFP and isolated stable P23 and P26 fragments by CD, differential scanning calorimetry, and immunopptn. techniques demonstrated that these fragments conserved native secondary, tertiary; and antigenic structure, characteristic of the intact mol. It was concluded that, free of ligands, the AFP mol. could be considered as a three-domain mol., in which two compact rigid domains (N-terminal domain I and C-terminal domain III) are connected by relatively labile domain II. The structure of domain II could be approximated by a "molten globule" state, characterized by the absence of rigid tertiary structure but having a pronounced secondary structure. Tumor-suppressive activity via induction of **apoptosis** was recently shown for AFP [Dudich, E. I., et al. (1998) Tumor Biol. 19, 261-272]. We studied here the ability of isolated proteolytic AFP fragments to induce **apoptosis** in the AFP-sensitive Raji cell line, to determine possible localization of the active site responsible for **apoptosis** signaling. Unlike intact AFP, neither isolated fragments nor their equimolar mixture was able to induce **apoptosis** in a human lymphoma Raji cell line. However, it was demonstrated that both fragments P23 or P26 and their equimolar mixture P23 + P26 operated synergistically with intact AFP in suppression of Raji cell proliferation. These data suggested that two structurally determined requirements are necessary for AFP-mediated triggering of **apoptosis**: (i) dimerization of AFP to form the heterodimeric complex of C- and N-terminal domains and (ii) participation of the central part of AFP mol. (domain II).

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2000:5091 CAPLUS Full-text
DOCUMENT NUMBER: 132:135712
TITLE: α-Fetoprotein causes **apoptosis** in tumor cells via a pathway independent of CD95, TNFR1 and TNFR2 through activation of caspase-3-like proteases
AUTHOR(S): **Dudich, Elena**; **Semenkova, Lidia**; **Dudich, Igor**; Gorbatova, Elena; Tochtamisheva, Natasha; **Tatulov, Edward**; Nikolaeva, Marina; Sukhikh, Gennady
CORPORATE SOURCE: Institute of Engineering Immunology, Lyubuchany, 142380, Russia
SOURCE: European Journal of Biochemistry (1999), 266(3), 750-761
CODEN: EJBCAI; ISSN: 0014-2956
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB α-Fetoprotein (AFP) is an oncoembryonal **protein** with multiple cell growth regulating, differentiating and immunosuppressive activities. Previous studies have shown that treatment of tumor cells in vitro with 1-10 μM AFP produces significant suppression of tumor cell growth by inducing dose-

dependent cytotoxicity, but the mol. mechanisms underlying these AFP functions are obscure. Here, the authors show that AFP cytotoxicity is closely related to **apoptosis**, as shown by cell morphol., nuclear DNA fragmentation and caspase-3-like activity resulting in cleavage of poly(ADP-ribose) polymerase. **Apoptosis** was significantly inhibited by a CPP32 family protease inhibitor whereas a general caspase inhibitor had no inhibitory effect, showing some enhancement of AFP-mediated **cell death**. Using fluorogenic caspase substrates, the authors found that caspase-3-like proteases were activated as early as 4 h after treatment of Raji cells with 15 μM AFP, whereas caspase-1, caspase-8, and caspase-9-like activity was not detected during the time interval 0.5-17 h. AFP treatment of Raji cells increased Bcl-2 **protein**, showing that AFP-induced **apoptosis** is not explained by downregulation of the Bcl-2 gene. This also suggests that AFP operates downstream of the Bcl-2-sensitive step. AFP notably decreased basal levels of soluble and membrane-bound Fas ligand. Incubation of AFP-sensitive tumor cells (HepG2, Raji) with neutralizing anti-Fas, anti-tumor necrosis factor receptor (TNFR)1 or anti-TNFR2 mAb did not prevent AFP-induced **apoptosis**, demonstrating its independence of Fas-dependent and TNFR-dependent signaling. In addition, it was found that cells resistant to TNF-induced (Raji) or Fas-induced (MCF-7) **apoptosis** are, nevertheless, sensitive to AFP-mediated **cell death** . In contrast, cells sensitive to Fas-mediated **cell death** (Jurkat) are completely resistant to AFP. Taken as a whole, the data demonstrate that: (a) AFP induces **apoptosis** in tumor cells independently of Fas/Fas ligand or TNFR/TNF signaling pathways, and (b) AFP-mediated **cell death** involves activation of the effector caspase-3-like proteases, but is independent of upstream activation of the initiator caspase-1, caspase-8, and caspase-9-like proteases.

REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 9 OF 12 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 1999-081276 [07] WPIX
DOC. NO. CPI: C1999-024522 [07]
TITLE: New catalytically active subunit of human telomerase - used in the modulation of telomerase activity, particularly for treating cancer and ageing
DERWENT CLASS: B04; D16
INVENTOR: HAGEN G; SIEGMUND H; WEICHEL W; WICK M; ZUBOV D
PATENT ASSIGNEE: (FARB-C) BAYER AG
COUNTRY COUNT: 81

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 9859040	A2	19981230	(199907)*	DE	76[9]	
AU 9882149	A	19990104	(199921)	EN		
DE 19816496	A1	19991021	(199950)	DE		
EP 990037	A2	20000405	(200021)	DE		
JP 2002508662	W	20020319	(200222)	JA	79	
AU 745420	B	20020321	(200233)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9859040	A2	WO 1998-EP3468	19980609
DE 19816496	A1	DE 1998-19816496	19980414
AU 9882149	A	AU 1998-82149	19980609

AU 745420 B	AU 1998-82149 19980609
EP 990037 A2	EP 1998-932142 19980609
EP 990037 A2	WO 1998-EP3468 19980609
JP 2002508662 W	WO 1998-EP3468 19980609
JP 2002508662 W	JP 1999-503685 19980609

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 745420 B	Previous Publ	AU 9882149 A
AU 9882149 A	Based on	WO 9859040 A
EP 990037 A2	Based on	WO 9859040 A
JP 2002508662 W	Based on	WO 9859040 A
AU 745420 B	Based on	WO 9859040 A

PRIORITY APPLN. INFO: DE 1998-19816496 19980414
DE 1997-19726329 19970620
DE 1998-19813274 19980326

AN 1999-081276 [07] WPIX

AB WO 1998059040 A2 UPAB: 20060114
Catalytically active human telomerase subunit (I), its functional equivalents, variants and catalytically active fragments are new. Also new are: (1) nucleic acid (II) encoding (I) and its functional equivalents; (2) antisense nucleic acid (IIa) that binds to (II); (3) antibodies (Ab) against (I), optionally labelled; (4) vectors containing (II); and (5) microorganisms containing this vector.
USE - Hosts of (5) are used to produce recombinant (I) which is used: (a) in screening assays to identify modulators of telomerase; and (b) to treat or inhibit cellular disorders, death, defects and/or other pathological processes involving telomerase, particularly cancer and ageing (also suitable for this are agents that stimulate, inhibit or mimic the activity of (I)). (IIa) inhibit telomerase action (by binding to specific mRNA), particularly in neoplastic cells and may be expressed in vivo . Ab, and fragments of (II), used as probes or primers, are used to diagnose telomerase-related conditions (especially neoplasia) by: (i) detecting abnormal levels of (I) in body fluids or tissues; or (ii) by measuring the amount of (I)-encoding nucleic acid.
ADVANTAGE - Expression of (I)-related mRNA is confined to tumour cells, in contrast to the ubiquitous expression of the telomerase RNA subunit.

Member(0003)

ABEQ DE 19816496 A1 UPAB 20060114
Catalytically active human telomerase subunit (I), its functional equivalents, variants and catalytically active fragments are new. Also new are: (1) nucleic acid (II) encoding (I) and its functional equivalents; (2) antisense nucleic acid (IIa) that binds to (II); (3) antibodies (Ab) against (I), optionally labelled; (4) vectors containing (II); and (5) microorganisms containing this vector.
USE - Hosts of (5) are used to produce recombinant (I) which is used: (a) in screening assays to identify modulators of telomerase; and (b) to treat or inhibit cellular disorders, death, defects and/or other pathological processes involving telomerase, particularly cancer and ageing (also suitable for this are agents that stimulate, inhibit or mimic the activity of (I)). (IIa) inhibit telomerase action (by binding to specific mRNA), particularly in neoplastic cells and may be expressed in vivo . Ab, and fragments of (II), used as probes or primers, are used to diagnose telomerase-related conditions (especially neoplasia) by: (i) detecting abnormal levels of (I) in body fluids or tissues; or (ii) by measuring

the amount of (I)-encoding nucleic acid.

ADVANTAGE - Expression of (I)-related mRNA is confined to tumour cells, in contrast to the ubiquitous expression of the telomerase RNA subunit.

Member(0004)
ABEQ EP 990037 A2 UPAB 20060114
Catalytically active human telomerase subunit (I), its functional equivalents, variants and catalytically active fragments are new. Also new are: (1) nucleic acid (II) encoding (I) and its functional equivalents; (2) antisense nucleic acid (IIa) that binds to (II); (3) antibodies (Ab) against (I), optionally labelled; (4) vectors containing (II); and (5) microorganisms containing this vector.

USE - Hosts of (5) are used to produce recombinant (I) which is used: (a) in screening assays to identify modulators of telomerase; and (b) to treat or inhibit cellular disorders, death, defects and/or other pathological processes involving telomerase, particularly cancer and ageing (also suitable for this are agents that stimulate, inhibit or mimic the activity of (I)). (IIa) inhibit telomerase action (by binding to specific mRNA), particularly in neoplastic cells and may be expressed in vivo . Ab, and fragments of (II), used as probes or primers, are used to diagnose telomerase-related conditions (especially neoplasia) by: (i) detecting abnormal levels of (I) in body fluids or tissues; or (ii) by measuring the amount of (I)-encoding nucleic acid.

ADVANTAGE - Expression of (I)-related mRNA is confined to tumour cells, in contrast to the ubiquitous expression of the telomerase RNA subunit.

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ACCESSION NUMBER:	1998-0051049 PASCAL Full-text
COPYRIGHT NOTICE:	Copyright .COPYRGT. 1998 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH):	Growth-regulative activity of human alpha-fetoprotein for different types of tumor and normal cells
AUTHOR:	DUDICH E.; SEMENKOVA L.; GORBATOVA E.; DUDICH I.; KHROMYKH L.; TATULOV E.; GRECHKO G.; SUKHIKH G.
CORPORATE SOURCE:	Institute of Engineering Immunology, Moscow Region, Russian Federation; Institute of Cancerogenesis, Russian Academy of Medicine, Moscow, Russian Federation; Moscow Clinical Hospital 31, Moscow, Russian Federation; Institute of Biological Medicine, Moscow, Russian Federation
SOURCE:	Tumor biology, (1998), 19(1), 30-40, 52 refs. ISSN: 1010-4283
DOCUMENT TYPE:	Journal
BIBLIOGRAPHIC LEVEL:	Analytic
COUNTRY:	Switzerland
LANGUAGE:	English
AVAILABILITY:	INIST-18298, 354000079773180040

AN 1998-0051049 PASCAL Full-text
CP Copyright .COPYRGT. 1998 INIST-CNRS. All rights reserved.
AB The dose-dependent α-fetoprotein (AFP) reactivity of different types of tumor cells and normal embryonal fibroblasts, which are capable of taking up AFP, was investigated. High doses (more than 100 µg/ml) of purified human AFP were shown to induce strongly dose-dependent growth inhibition ofhuman hepatoma HepG2 cells, human lymphoblastoma MT4 cells, lymphoma Jurkat cells and murine

fibroblastoma L929 cells. Human mammary carcinoma MCF-7 cells also revealed a growth inhibitory response to AFP, although to a lesser extent. Equivalent doses of human serum albumin (HSA) demonstrated no effect on these cells. On the contrary, normal embryonal fibroblasts of different organ origin showed dose-dependent stimulation (50-90%) of proliferation in response to AFP. A similar stimulative effect was obtained when embryonal fibroblasts were treated with the same doses of HSA. The myeloblastoma cell line U-937 and the normal epidermal fibroblast cell line M19 were shown to be resistant to the AFP action over a wide range of **protein** concentrations. It was demonstrated that growth factor deprivation (i.e. low serum concentration) could stimulate U-937 cell proliferation in response to high doses of AFP. It was also shown that intensive washing of U-937 and MCF-7 cells with fresh medium to remove secreted cytokines and growth factors distinctly increased cell sensitivity to high-dose-AFP-induced growth-inhibitory activity. Low AFP concentrations (less than 100 μg/ml) failed to induce growth inhibition in all studied cells and rather showed a slight stimulative effect. These findings demonstrate that physiological levels of AFP can exhibit a dose-dependent growth-regulatory activity toward sensitive tumor or developing cells. Our data demonstrated that AFP could reveal either stimulative or inhibitory growth activity, depending on the relative concentration of AFP and on exogenous or endogenous cytokines and growth factors in the cell culture medium. A growth-stimulative activity in normal embryonal fibroblasts and certain tumor cell lines exhibited by low AFP concentrations is supposed to result from the synergistic effects of AFP and various other secreted growth factors.

L29 ANSWER 11 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1999:109040 BIOSIS Full-text
DOCUMENT NUMBER: PREV199900109040
TITLE: AFP-mediated **apoptosis** is realized via Ca2+ and tyrosine-kinase independnet pathways and do not require **protein** and RNA synthesis.
AUTHOR(S): **Semenkova, Lydia; Dudich, Elena;** Khromikh, Ludmila; Gorbatova, Elena
CORPORATE SOURCE: Inst. Eng. Immunol., Lyubuchany, Moscow Region, Checkhov District 142380, Russia
SOURCE: Tumor Biology, (Aug., 1998) Vol. 19, No. SUPPL. 2, pp. 26. print.
Meeting Info.: 26th Meeting of the International Society for Oncodevelopmental Biology and Medicine. Umea, Sweden. August 30-September 4, 1998.
ISSN: 1010-4283.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Mar 1999
Last Updated on STN: 4 Mar 1999

L29 ANSWER 12 OF 12 MEDLINE on STN DUPLICATE 6

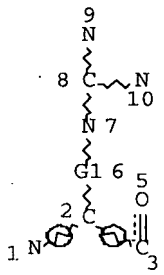
ACCESSION NUMBER: 97421909 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 9276026
TITLE: Induction of **apoptosis** in human hepatoma cells by alpha-fetoprotein.
AUTHOR: **Semenkova L N; Dudich E I;** **Dudich I V**
CORPORATE SOURCE: Institute of Engineering Immunology, Lyubuchany, Russia.
SOURCE: Tumour biology : the journal of the International Society for Oncodevelopmental Biology and Medicine,

(1997) Vol. 18, No. 5, pp. 261-73.
Journal code: 8409922. ISSN: 1010-4283.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 26 Sep 1997
Last Updated on STN: 26 Sep 1997
Entered Medline: 17 Sep 1997

AB We have investigated the effects of purified human alpha-fetoprotein (AFP) on the growth of the human hepatocarcinoma-cells HepG2 in culture. Cancer-derived AFP (cAFP), isolated from the culture medium of AFP-secreting HepG2 cells and embryonal AFP (eAFP), isolated from human cord serum, were used for these studies. Both AFP pre parations studied were shown to induce strong dose-dependent inhibition of HepG2 cell proliferation and complete growth arrest at high **protein** concentrations (more than 0.1 mg/ml). To test whether AFP may trigger an endogenous suicide program in hepatoma cells, we examined whether DNA fragmentation preceded **cell death**. After exposure of the cells of the high AFP dose (1.0 mg/ml), DNA fragmentation was detected as early as 2 h after treatment, and 70% of cells were **apoptotic** by 24 h. DNA fragmentation was shown to precede other signs of **cell death** for several hours. Typical morphological changes of **apoptosis** were observed after 4 h of exposure of cells to high AFP doses. Low concentrations of cAFP and eAFP (less than 0.1 mg/ml) failed to induce growth inhibition of HepG2 cells, rather showing a weak stimulative effect, demonstrating a biphasic AFP activity. Cell pretreatment with the transcriptional inhibitor actinomycin D had no measurable influence on AFP cytotoxicity. These findings demonstrate that **protein** synthesis is not required for this mechanism of **cell death**. The charcoal-treated ligand-free eAFP (eAFPp) had a dose-dependent growth-inhibitory activity, similar to intact **protein**, but slightly less intensive. The similar growth-inhibitory activities of cAFP, eAFP and eAFPp, which have a significant difference in bound-ligand content, provide evidence that the main role in cell growth regulation may be attributed to the **protein** moiety of the entire AFP molecule, but not to its ligands. These biologically active AFP ligands could, however, modulate AFP-growth-regulating activity. Growth factor deprivation distinctly enhanced the cytostatic activity of high AFP concentrations and also increased the mitogenic activity of low AFP levels, showing the interdependence of the growth-regulative activity of AFP and growth factors. The findings of this study demonstrated that AFP is directly introduced into the intracellular pathways of cell growth regulation and programmed **cell death**.

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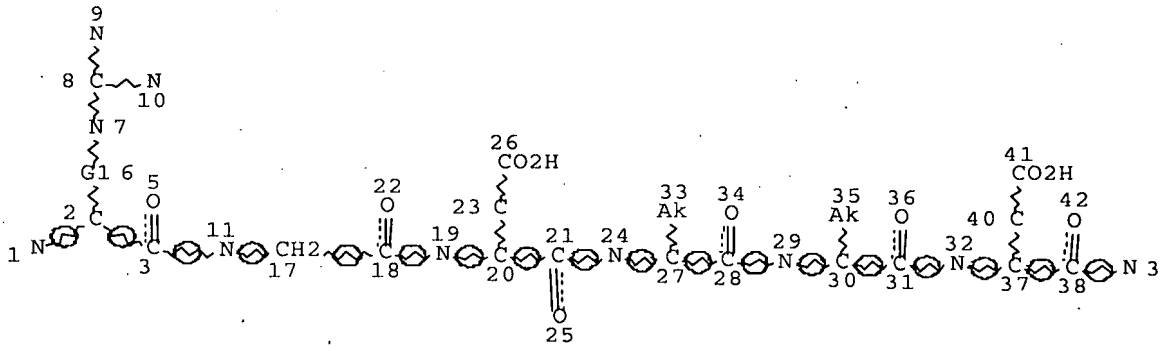
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 9

STEREO ATTRIBUTES: NONE
L7 (19673) SEA FILE=REGISTRY SSS FUL L6
L8 STR



Page 1-A

9

Page 1-B
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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 36

STEREO ATTRIBUTES: NONE

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L5            0 SEA ABB=ON  PLU=ON  L1

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                SAV TEMP L14 HAJ5307C/A
                ACT HAJ5307C/A
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L8              STR
L9            7 SEA SUB=L7 SSS FUL L8
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     FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 16:27:06 ON 21 AUG 2007
L13           0 SEA ABB=ON  PLU=ON  L9

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     AT 16:30:45 ON 21 AUG 2007
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L18          71 SEA ABB=ON  PLU=ON  "ZUBOV D"?/AU
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L23          43 SEA ABB=ON  PLU=ON  L16 AND (L17 OR L18 OR L19)
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                APOPTOT? OR (CELL OR CELLULAR)(3A) DEATH)
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L28          28 SEA ABB=ON  PLU=ON  L20 OR L25 OR L27
L29          12 DUP REM L28 (16 DUPLICATES REMOVED)
               D 1-12 IBIB ABS
               D QUE L9


FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

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DICTIONARY FILE UPDATES:  20 AUG 2007  HIGHEST RN 945102-95-4

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 FILE LAST UPDATED: 18 Aug 2007 (20070818/UP).  FILE COVERS 1950 TO DA

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  substance identification.

FILE BIOSIS
FILE COVERS 1926 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
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FROM JANUARY 1926 TO DATE.

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FILE EMBASE
FILE COVERS 1974 TO 21 Aug 2007 (20070821/ED)

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE WPIX
FILE LAST UPDATED: 17 AUG 2007 <20070817/UP>
MOST RECENT THOMSON SCIENTIFIC UPDATE: 200753 <200753/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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>>> Indian patent publication number format enhanced in DWPI - see NEW

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